

THE CLAIMS

What is claimed is:

- 1. A method of combating movement disorder in a patient experiencing or susceptible to same, by administering to the patient an effective amount of a neurotransmission modulating composition comprising a 5HT antagonist and/or α_2 antagonist.
- 2. The method of claim 1, wherein the composition comprises a 5HT antagonist.
- 3. The method of claim 1, wherein the composition comprises a 5HT antagonist including at least one of 5HT2 antagonists and 5HT3 antagonists.
- 4. The method of claim 1, wherein the composition comprises an α_2 antagonist.
- 5. The method of claim 1, wherein the composition comprises a compound that is both a 5HT antagonist and an α_2 antagonist.
- 6. The method of claim 1, wherein said movement disorder comprises dyskinesia.
- 7. The method of claim 1, wherein said movement disorder comprises a condition selected from the group consisting of tremors, akathisias, asterixis, athetosis, choreaathetosis, tics, chorea/choreaform movements, dystonias, spasticity, restless legs syndrome, hyperkinetic movement disorders, hemiballismus, myoclonus, and tardive dyskinesia.



- 8. The method of claim 1, wherein said movement disorder comprises tremor.
- 9. The method of claim 1, wherein said movement disorder comprises a peripheral neuropathy-associated tremor.
- 10. The method of claim 1, wherein said movement disorder comprises at least one tremor condition selected from the group consisting of Parkinsonian tremors, rubral tremors, post-traumatic tremors, drug-induced tremors, cerebellar tremors, and Tourette syndromal tremors.
- 11. The method of claim 1, wherein said movement disorder derives from neurological impairment of the basal ganglia.
- 12. The method of claim 1, wherein said movement disorder comprises a disorder selected from the group consisting of Parkinsonian tremor, action tremor and levodopa-induced dyskinesias.
- 13. The method of claim 1, wherein said composition comprises at least one compound selected from the group consisting of:
- (a) tetracyclic compounds of the formula:



or a salt thereof, wherein

A represents a pyridine ring or a halogen substituted pyridine ring,

R₁ represents hydrogen, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkylthio, halogen, OH, SH or CF₃,

 R_2 represents hydrogen or a lower alkyl or aralkyl group, and n and m may each be 1, 2 or 3 with the proviso that the sum of m and n must be 2, 3 or 4;

- (b) imidazolines;
- (c) ergot alkaloids; and
- (d) indolealkylamine alkaloids.
- 14. The method of claim 1, wherein said composition comprises at least one tetracyclic compound of the formula:



or a salt thereof, wherein

A represents a pyridine ring or a halogen substituted pyridine ring,

R₁ represents hydrogen, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkylthio, halogen, OH, SH or CF₃,

 R_2 represents hydrogen or a lower alkyl or aralkyl group, and n and m may each be 1, 2 or 3 with the proviso that the sum of m and n must be 2, 3 or 4.

15. The method of claim 1, wherein said composition comprises an α_2 antagonist selected from the group consisting of:

atipamezole;

idazoxan;

imiloxan;

N-(2-(N-Methanesulfonamido-2,3-dihydroindol-5-yl)ethyl)(-N-((R)-(+)-5-methox)-1,2,3,4-tetrahydronaphthalen-1-ylmethyl)-N-methylamine;

N-(2,3-Dihydroindol-5-yl)ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-ylmethyl)-N-methylamine;

N-(2-(N-Methanesulfonamido-2,3-dihydroindol-6-yl)ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-ylmethyl)-N-methylamine;

N-(2-(N-Propanesul fonamido-2,3-dihydroindol-6-yl) ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-ylmethyl)-N-methylamine;

N-(2-(N-Isobutane sulfonamido-2,3-dihydroindol-6-yl)ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-ylmethyl)-N-methylamine;

N-(2-(N-Methyl-2,3-dihydroindol-5-yl)ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)-N-methylamine;

N-(2-(N-Methyl-2,3-dihydroindol-6-yl)ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-ylmethyl)-N-methylamine;

N-(2-(2,3-Dihydroindol-6-yl)ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-ylmethyl)-N-methylamine;

N-(2-(2,3-Dihydroindol-5-yl)ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahydronaphthalen-1,2,3,4-tetrahyd



1-ylmethyl)-N-methylamine;

N-(2-(Indol-6-yl)ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-ylmethyl)-N-methylamine;

N-(2-(N-Methanesulfondamido-1,3-dihydroisoindol-5-yl)ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-ylmethyl)-N-methylamine;

N-(2-(N-Methyl-1,3-dihydroisoindol-5-yl)ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4 - tetrahydronaphthalen-1-ylmethyl)-N-methylamine;

N-(2-(1,3-Dihydroisoindol-5-yl)ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydronaphthalen-1-ylmethyl)-N-methylamine;

N-(2-(N-Methyl-2,3-dihydro-1H-indol-5-yl)-ethyl(-N-((R)-(+)-5-methoxy-1,2,3,4-tetrahydro-naphthalen-1-ylmethyl)-N-methylamine; and

5-{2-(((R)-(+)-5-Methoxy-1,2,3,4-tetrahydro-naphthalen-1-ylmethyl)methylamino)-ethyl}-1,3-dihydro-indol-2-one.

16. The method of claim 1, wherein said composition comprises a 5HT antagonist including a therapeutic agent selected from the group consisting of ergonovine (Ergotrate), pizotifen, mianserin, Ketanserin (Sufrexal), Ondansetron (Zofran), ritanserin, clozapine (Clozaril), risperidone (Risperdal), methysergide (Sansert), and cyproheptadine (Periactin).



17. The method of claim 1, wherein said 5HT antagonist comprises a therapeutic agent selected from the group consisting of

indol-3-yl-carboxylic acid-endo-8-methyl-8-aza-bicyclo[3,2,1]-oct-3-yl-ester;

benzo[b]thiophen-3-yl-carboxylic acid-endo-9-methyl-azabicyclo-[3,3,1]non-3-yl-ester;

5-fluoro-1-methyl-indol-3-yl-carboxylic acid-endo-9-methyl-9-aza-bicyclo[3,3,1]non-3-yl-ester;

1,2,3,9-tetrahydro-9-methyl-3-[(2-methyl-1H-imidazol-1-yl)-methyl-4H-carbaz ol-4-one;

1-methyl-indazol-3-yl-carboxylic acid-9-methyl-9-aza-bicyclo-[3,3,1]-non-3.alpha.-yl-amide;

endo-4-amino-5-chloro-2-methoxy-N-(1-azabicyclo[3,3,1]non-4-yl)-benzamide; and

3-[5-methyl-1H-imidazol-4-yl]-1-(1-methyl-1H-indol-3-yl)-1-propanone.

- 18. The method of claim 1, wherein the composition comprises a presynaptic α_2 antagonist and a postsynaptic 5HT antagonist.
- 19. The method of claim 1, wherein the composition comprises mirtazapine.

- 20. The method of claim 19, wherein mirtazapine is administered orally to the patient.
- 21. The method of claim 20, wherein mirtazapine is administered orally in a dose of from about 10 to about 100 milligrams per day.
- 22. The method of claim 20, wherein mirtazapine is administered orally in a dose of from about 15 to about 60 milligrams per day.
- 23. The method of claim 1, wherein the composition comprises a noradrenergic and serotonergic neurotransmission-modulating agent.
- 24. The method of claim 1, wherein the composition does not mediate sedation in dosages effective for combating movement disorder.
- A method of combating movement disorder in a patient experiencing or susceptible to same, comprising administering to the patient an effective amount of a piperazinoazepine compound that is a receptor antagonist for at least one receptor selected from the group consisting of 5HT and α_2 receptors.
- 26. A method of combating movement disorder in a patient experiencing or susceptible to same, comprising administering to the patient an effective amount of a serotonergic antagonist for at least one receptor selected from the group consisting of 5HT and α_2 receptors.

- 27. The method of claim 26, wherein said serotonergic antagonist is a SHT2 and/or SHT2 and/or SHT2 antagonist.
- 28. The method of claim 27, wherein said 5HT2 and/or 5HT3 antagonist is concurrently an α_2 receptor antagonist.
- 29. The method of claim 26, wherein said serotonergic antagonist comprises mirtazapine.
- 30. The method of claim 26, wherein said movement disorder comprises Parkinsonian tremor.